UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JAMES W. WILLIAMS,
ANITA CHONG and W. JAMES WALDMAN

Appeal No. 2005-0902
Application No. 09/529,053

ON BRIEF

Before ELLIS, MILLS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 16-25, all of the claims remaining. Claims 16, 22, and 25 are representative and read as follows:

> 16. A method for inhibiting viral replication in cells susceptible to viral infection comprising contacting said cells with a leflunomide product in an amount effective to inhibit viral virion assembly.
>
> 22. The method of claim 16 further comprising contacting the cells with another anti-viral agent.
>
> 25. The method of claim 16 wherein cells are virally infected.

The examiner relies on the following references:

Weithmanǹn et al. (Weithmann)	5,556,870	Sep. 17, 1996
Coghlan et al. (Coghlan)	WO 94/24095	Oct. 27, 1994

McChesney et al. (McChesney), "An Evaluation of Leflunomide in the Canine Renal Transplantation Model," Transplantation, Vol. 57, No. 12, pages 1717-1722 (1994).

Flamand et al. (Flamand), "Human Herpesvirus 6 Induces Interleukin-1ß and Tumor Necrosis Factor Alpha, but Not Interleukin-6, in Peripheral Blood Mononuclear Cell Cultures," Journal of Virology, Vol. 65, No. 9, pages 5105-5110 (1991).

Hammer, "Advances in Antiretroviral Therapy and Viral Load Monitoring," AIDS, Vol. 10 (suppl. 3), pages S1-S11 (1996).

Claims 16-21, 24, and 25 stand rejected under 35 U.S.C. § 103 as obvious in view of Coghlan and McChesney.

Claims 22 and 23 stand rejected under 35 U.S.C. § 103 as obvious in view of Coghlan, McChesney, and Hammer.

Claims 16, 17, 20, 21, 24, and 25 stand rejected under 35 U.S.C. § 103 as obvious in view of Weithmann.

Claims 22 and 23 stand rejected under 35 U.S.C. § 103 as obvious in view of Weithmann and Hammer.

Claim 19 stands rejected under 35 U.S.C. § 103 as obvious in view of Weithmann and Flamand.

We affirm the rejection based on Coghlan and McChesney and the rejection based on Weithmann and Hammer. We do not reach the remaining rejections.

Background

Leflunomide (HWA-486) is a known product, as is its metabolite A771726. See the specification, page 1. "Leflunomide originated from a series of compounds that were designed as agricultural herbicides. . . . It was later found to have anti-inflammatory and immunosuppressive activity, and it has been evaluated in animal models of autoimmune disease and transplant rejection. . . . No anti-viral activity has previously been reported for leflunomide or its metabolite." Id., pages 1-2.

The specification discloses that "[l]eflunomide has been discovered to inhibit viral growth in a manner different from other conventional anti-viral agents, which typically act by inhibiting viral DNA replication in the early stages of infection. In contrast, leflunomide appears to act by inhibiting virion assembly." Page 13.

Discussion

The claims subject to each rejection stand or fall together, because Appellants have not stated otherwise. See the Appeal Brief, page 3. We will focus on claim 16 as representative of the claims rejected over Coghlan and McChesney and claim 22 as representative of the claims rejected over Weithmann and Hammer.

1. Claim construction

Claim 16 is directed to a "method for inhibiting viral replication in cells susceptible to viral infection" by contacting the cells with a "leflunomide product" in an amount "effective to inhibit viral virion assembly." Claim 22 is directed to the same method, "further comprising contacting the cells with another anti-viral agent."

The specification defines "leflunomide product" to mean "leflunomide . . . (HWA-486), or its active metabolite . . . (A771726), or related derivatives . . . or metabolites

thereof that retain all or part of the anti-viral activity of leflunomide." Page 18, lines

12-18. Regarding effective doses of leflunomide, the specification states:

> Anti-viral therapeutically effective amounts of leflunomide product include amounts effective for inhibiting viral growth, i.e., replication, or inhibiting virion assembly. The leflunomide product can be administered to humans at doses ranging from about 0.1 to 80 mg daily, varying in children and adults, or more preferably at doses ranging from about 15 to 25 mg daily for adults. Most preferable are doses calculated to provide a circulating blood level of about 40 to 60 µM.

Page 16, lines 17-23.

Reading the claims in light of the specification, therefore, we construe claim 16 to require administration of leflunomide, its active metabolite, related derivatives, or anti-virally active metabolites thereof, in an amount that is effective to inhibit viral growth or viral assembly; such amounts can vary from 0.1 mg/day to 80 mg/day for a human.

We do not interpret claim 16 to require administering leflunomide to a patient; i.e., in vivo administration. Claim 16 requires only contacting a cell that is susceptible to viral infection with a leflunomide product. It does not require administering a leflunomide product to a patient or a human or an animal. During examination, claims are given their broadest reasonable interpretation. See In re Morris, 127 F.3d 1048, 1053-54, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). Since claim 16 is not expressly limited to an in vivo method, the broadest reasonable interpretation of the claim is that it also reads on in vitro methods.

We also do not interpret claim 16 to be limited to a method of treating cells that are already infected by viruses. Claim 25 adds to claim 16 the limitation that the "cells are virally infected." Since a dependent claim must further limit the claim from which it

depends, see 35 U.S.C. § 112, fourth paragraph, that limitation by implication is not present in claim 16.

Finally, we conclude that the preamble of claim 16 – "for inhibiting viral replication in cells susceptible to viral infection" – requires only that the cells contacted with a leflunomide product are susceptible to viral infection. It does not require that the contacting be done with the intent of inhibiting viral infection. Rather, the preamble phrase "for inhibiting viral replication" merely recites the purpose or intended use of the claimed method and therefore is not a positive limitation. See Pitney Bowes Inc. v. Hewlett Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165-66 (Fed. Cir. 1999):

> If the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the claim preamble is 'necessary to give life, meaning, and vitality' to the claim, then the claim preamble should be construed as if in the balance of the claim. . . . If, however, the body of the claim fully and intrinsically sets forth the complete invention, including all of its limitations, and the preamble offers no distinct definition of any of the claimed invention's limitations, but rather merely states, for example, the purpose or intended use of the invention, then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation.

See also Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 1368, 1376, 58 USPQ2d 1508, 1513 (Fed. Cir. 2001) (Preamble reciting "a method for treating a cancer patient to effect regression of a taxol-sensitive tumor, said method being associated with reduced hematologic toxicity" was "only a statement of purpose and intended result. The expression does not result in a manipulative difference in the steps of the claim.").

Thus, we construe claim 16 to be directed to a method comprising contacting cells susceptible to viral infection with, e.g., leflunomide or its active metabolite in an amount effective to inhibit virion assembly, either in vitro or in vivo. We construe claim 22 to be directed to the same method, where the cells are also contacted with another antiviral agent in addition to the leflunomide product.

2. Coghlan and McChesney

The examiner rejected claims 16-21, 24, and 25 as obvious in view of Coghlan and McChesney. We conclude that McChesney anticipates claim 16, as we interpret it, so we need not address Coghlan.

McChesney describes an experiment in which dogs weighing 10-30 kg were administered either leflunomide or its active metabolite (A77-1726). See the paragraph bridging pages 1717 and 1718, and the first paragraph on page 1718. The dogs treated with leflunomide received 2, 4, 8, or 16 mg/kg/day; the dogs treated with A77-1726 received 2, 4, 6, or 8 mg/kg/day. See the second full paragraph on page 1718. The dosages described by McChesney therefore correspond to between 20 and 480 mg/day of leflunomide and 20-240 mg/day of A77-1726.[1]

Thus, McChesney describes in vivo administration of leflunomide and its active metabolite at dosages within the range taught in the instant specification to be effective for inhibiting virion assembly. McChesney therefore anticipates claim 16. Anticipation is the epitome of obviousness. See Connell v. Sears, Roebuck & Co., 722 F.2d 1542, 1548, 220 USPQ 193, 198 (Fed. Cir. 1983).

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[1] The calculated dosages correspond to the lightest dog at the lowest dose and the heaviest dog at the highest dose for each drug.

> Appellants argue that
>
> McChesney shows immunosuppressive effects of leflunomide alone and with cyclosporine in canines with kidney allograft transplants. . . . The McChesney reference includes no experimental procedures for assessing antiviral or antibacterial effects of leflunomide.
>
> Clearly, then, the combined Coghlan and McChesney references provide no suggestion whatsoever in their disclosures to those of ordinary skill in the art that leflunomide products had been found to be effective in inhibiting viral virion assembly or might be tested for such effects with any reasonable expectation of success.

Appeal Brief, page 11.

Appellants' arguments are based on an incorrect interpretation of the claim: claim 16 does not require administering leflunomide with the expectation of obtaining an antiviral effect. Appellants may have recognized a new benefit of administering leflunomide to patients but claim 16 as written reads on prior art processes. See In re Woodruff, 919 F. 2d 1575, 1578, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990): "It is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable."

3. Weithmann and Hammer

The examiner rejected claims 22 and 23 as obvious in view of Weithmann and Hammer. The examiner noted that Weithmann teaches treating viral disorders, including HIV infection, by administering leflunomide at doses of 3-50 mg daily. See col. 2, lines 4-10 and 34-37; col. 3, lines 7-10; and claim 1.

Weithmann does not teach administering leflunomide in combination with another antiviral agent, but Hammer discloses several antiviral agents used to treat HIV infection. See, in particular, Figure 2, which shows several reverse transcriptase inhibitors: all of the compounds shown except didanosine are pyrimidine analogs.

Hammer also teaches that combination therapy for HIV provides several advantages over treatment with a single antiviral drug. See page s2, paragraph bridging the columns.

In view of these teachings, it would have been obvious to a person of ordinary skill in the art, at the time the invention of claim 22 was made, to administer leflunomide at 3 to 50 mg per day to a patient having an HIV infection, in combination with one of the other antiretroviral agents described by Hammer (e.g., zidovudine in Figure 2). Motivation to do so is provided by Hammer, who teaches that treating HIV infection with a combination of antiviral agents is expected "(1) to provide additive or synergistic antiviral activity; (2) to modulate, and hopefully prevent, the emergence of resistance; (3) to minimize toxicity; and (4) to provide drug activity in different cellular and body compartments." We therefore agree with the examiner that the teachings of Weithmann and Hammer would have made obvious the invention of claim 22.

Appellants argue that

> [c]laim 23 is directed to co-administration of leflunomide products with a pyrimidine. Leflunomide products inhibit dihydroorotate dehydrogenase, a key enzyme in the biosynthesis of pyrimidines. Appellants disclose and claim the co-administration of leflunomide products with a pyrimidine, "in order to reduce its [the leflunomide products'] potential toxicity while maintaining its therapeutic effectiveness." (Pages 20-21 of the Application)[.]
>
> Neither Weithmann nor Hammer have <u>any</u> discussion of co-administering a pyrimidine with leflunomide (or with any anti-viral agent) to <u>stimulate</u> DNA synthesis. Rather, the various nucleoside analogue reverse transcriptase inhibitors . . . are taught to <u>prevent</u>, as opposed to <u>facilitate</u>, DNA synthesis. Since Hammer teaches the opposite effect of that stated by the Appellants, one of ordinary skill in the art would not have combined Hammer with Weithmann.

Appeal Brief, page 9 (alterations in original).

This argument is not persuasive. Whether the prior art references suggest combining their teachings for the same reason Appellants made their combination is immaterial. Rather, "[w]hen determining the patentability of a claimed invention which combines two known elements, 'the question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination.'" In re Beattie, 974 F.2d 1309, 1311-12, 24 USPQ2d 1040, 1042 (Fed. Cir. 1992) (emphasis added). Here, both prior art references concern treatment of HIV: Weithmann teaches that leflunomide is useful in treating HIV infections, while Hammer teaches other anti-HIV agents and suggests that a combination of anti-HIV agents is more effective than a single agent. These teachings reasonably suggest the method defined by claim 22.

Summary

We affirm the rejection of claims 16-21, 24, and 25, based on Coghlan and McChesney. We also affirm the rejection of claims 22 and 23 based on Weithmann and Hammer. In both cases, however, since our reasoning differs somewhat from that of the examiner, we designate our affirmance a new ground of rejection under 37 CFR § 41.50(b).

Time Period for Response

This decision contains a new ground of rejection pursuant to 37 CFR § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 CFR § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 CFR § 41.50(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution*. Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . .
>
> (2) *Request rehearing*. Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

AFFIRMED, 37 CFR § 41.50(b)

JOAN ELLIS)
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